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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,243	07/16/2001	Alexander H. Taylor	P50770X1C1	4165

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08/13/2003

GLAXOSMITHKLINE
Corporate Intellectual Property - UW2220
P.O. Box 1539
King of Prussia, PA 19406-0939

EXAMINER: [Signature]

HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 08/13/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/905,243

Applicant(s)

TAYLOR, ALEXANDER H.

Examiner

Larry R. Helms

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 40-63 is/are pending in the application.
- 4a) Of the above claim(s) 53-58 and 63 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 40-47, 50 and 62 is/are rejected.
- 7) ☒ Claim(s) 48, 49, 51, 52 and 59-61 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s) _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Request for Continued Examination

1. The request filed on 5/20/03 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/905243 is acceptable and a RCE has been established. Claims 40-63 are pending. An action on the RCE follows.
2. Claims 1-39 have been canceled.
Claims 40-63 have been added.
3. Claims 40-52 and 59-62 are under examination and will be examined to the extent the species of Pan troglodytes is the elected species of Old World apes.
4. Newly submitted claims 53-58 and 63 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:
Claims 53-58 are directed to frameworks from cynomolgus which was in Group II in the original restriction requirement mailed 3/12/02 and claim 63 is directed to a method that was in Group III in the original restriction requirement mailed 3/12/02.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 53-58 and 63 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

5. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.
6. The following Office Action contains some NEW GROUNDS of rejection.

Rejections Withdrawn

7. The rejection of claims under 35 U.S.C. 103(a) as being unpatentable over Newman et al (U.S. Patent 5,756,096, filed 6/7/95) and further in view of Vijn-Warrier et al (Molecular Immunology 32:1081-1092, 1995, IDS #7) and Adair et al (WO 91/0996, published 7/11/91) is withdrawn in view of the amendments to the claims.

The following are NEW GROUNDS of rejections

Claim Rejections - 35 USC § 112

8. Claim 46 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 46 is indefinite for reciting "an analog of an amino acid" because the exact meaning of the phrase is not clear. It is not clear what an "analog" of an amino acid is. Is an analog of TYR, PHE or is an analog a peptide mimetic or some other meaning?

Claim Rejections - 35 USC § 103

9. Claims 40-47, 50, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adair et al (WO 91/09967, published 7/91, PTO-892, paper #6) and further in view of Vijn-Warrier et al (Molecular Immunology 32:1081-92, 1995, PTO-892, paper #6).

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The claims recite an antibody comprising CDRs from a mouse or rat and framework regions from Pan troglodytes and an antibody that has frameworks from pan troglodytes such that the frameworks do not influence CDR presentation.

Adair et al teach methods of CDR grafting comprising acceptor framework and donor antigen binding regions of rodent antibodies (see abstract). Adair et al also teach non-CDR residues which contribute to antigen binding and CDR contacting residues (see pages 20-23). Adair et al does not teach that the framework residues be from Pan troglodytes. This deficiency is made up for in the teachings of Vijn-Warrier.

Vijn-Warrier et al teach the nucleotide and amino acid sequence of the variable region of a Pan troglodytes antibody (see abstract). Vijn-Warrier also teach several human germline variable region genes (see Figure 3, 4, and 5, and Table 1) and that chimpanzee mAbs are no more likely to elicit deleterious anti-immunoglobulin responses in humans than human mAbs (see page 1089).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an antibody comprising donor CDRs from a rodent species and acceptor framework residues from Pan troglodytes in view of Adair et al and Vijn-warrier et al.

One of ordinary skill in the art would have been motivated to and have a reasonable expectation of success to produce the claimed invention because Vijn-Warrier et al teach "these findings suggest that chimpanzee mAbs are no more likely to elicit deleterious anti-immunoglobulin responses in humans than are human mAbs" (see page 1089) and that the chimpanzee VH and Vk genes are no more divergent than the

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human genes. In addition, one of ordinary skill in the art would have been motivated to produce the claimed invention because Adair et al teach donor CDRs from non-human species such as rodents (see abstract and page 8, lines 3-7) and Adair et al teach a method comprising retaining residues that are involved with antigen binding or contacting the CDRs or replacing solvent exposed framework residues (see pages 20-23, 38-39, and Figure 3). Thus, it would have been prima facie obvious to have used the framework regions from a Pan troglodyte to produce the claimed antibody due to the high homology between human and Pan troglodytes immunoglobulin amino acid sequences and combine the teachings of Adair who has produced antibodies with rodent CDRs and combine this with chimpanzee frameworks due to the high homology between chimpanzee mAbs and human mAbs as taught by Vijh-Warrier et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

The response filed 5/20/03 has been carefully considered but is deemed not to be persuasive. The response states that Vijh-Warrier et al merely suggest producing mAbs in chimpanzees for reduced immunogenicity and does not suggest developing mAbs in rodents and then altering them to resemble old world apes (see page 7 of response) and Adair et al does not suggest frameworks corresponding to Old world apes to reduce immunogenicity in humans (see page 8 of response). In response to these arguments, Vijh-Warrier et al clearly teach the similarities of human and chimpanzee antibodies and that chimpanzee antibodies would not be anymore immunogenic than human mAbs. Thus it would be obvious that the frameworks that

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comprise the antigenic regions of the antibody or at least the majority would be replaced in a rodent as taught by Adair et al to reduce the immunogenicity in a human with chimpanzee frameworks which as taught by Vijn-Warrier et al are almost identical to human frameworks and still low in immunogenicity.

Conclusions

10. No Claims are allowed. Claims 48-49, 51-52, 59-61 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3559. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the

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Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879



LARRY R. HELMS, PH.D.
PRIMARY EXAMINER